REMARKS

Status Summary

Claims 12 and 24-27 were previously pending in the present application. New claims 28-32 have been added by the present amendment.

Claims 12 and 24-27 have been rejected under 35 U.S.C. § 102(a) by the U.S. Patent & Trademark Office (hereinafter, "the Patent Office") as allegedly being anticipated by the journal article to Jonuleit *et al.* (*J. Exp. Med.* (2000), vol. 192(9): 1213-1222; hereinafter "Jonuleit *et al.*"). Claims 12 and 24-27 have also been rejected under 35 U.S.C. § 102(e) by the Patent Office as allegedly being anticipated by U.S. Patent No. 6,803,036 to Horwitz *et al.* (hereinafter "Horwitz *et al.*"). Claims 12 and 24-27 have also been rejected by the Patent Office under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

Claim 24 has been amended to correct a typographical error. Claims 12 and 24 have been amended to recite that the claimed method comprises contacting the human blood with ligands specifically binding to the CD4 and CD25 entities on the T cells, and/or CTL-A4 entities. Support for these amendments can be found in the specification, for example, on page 4, lines 25-32, in working Example 1 beginning on page 19, and in Figure 1A. No new matter has been added.

Reconsideration of the claims is respectfully requested.

Foreign Priority Claim

The Patent Office has acknowledged applicants' claim to foreign priority of the present application and noted that a certified copy of the foreign application has not yet been filed, as required by 35 U.S.C. § 119(b). A certified copy of the foreign priority document is enclosed.

Applicants note that the priority claim of the present application incorrectly listed the foreign priority document as a German patent application, when in actuality the foreign priority document is a European patent application having the same serial

number. Applicants have corrected this typographical error in the priority claim in the present Amendment.

Amendments to the Specification

Applicants have amended the specification to correct several instances of a typographical error in which CTL-A4 was referred to as "CD154", rather than "CD152" as listed elsewhere in the present application and as is understood within the field as the preferred CD designation for CTL-A4. The designation "CD154" is generally understood by those of skill in the art to reference CD40 ligand.

Support for the amendment can be found throughout the specification in which CTL-A4 is correctly referred to as CD152, and in particular at pages 2, 3, 11, and in Example 2 on page 21. The specification further supports the term "CD154" as referencing CD40 ligand at page 21 of the present application.

Response to 35 U.S.C. § 102 Claim Rejections

A. Jonuleit *et al.*

Claims 12 and 24-27 stand rejected by the Patent Office under 35 U.S.C. § 102(a) as being anticipated by Jonuleit *et al.* Applicants respectfully disagree with the assertions of the Patent Office and traverse the rejection.

Applicants note that claim 12 (and thus also claims 24-27, which depend from claim 12) has been amended to recite that the human blood is contacted with ligands specifically binding to the CD4 and CD25 entities on the T cells. Applicants respectfully submit that Jonuleit *et al.* does not teach the claimed subject matter of a method to identify, monitor and/or remove $CD4^+$ $CD25^+$ regulatory T cells from human blood. Instead, applicants respectfully submit Jonuleit *et al.* at best teaches the induction of regulatory T cells from human naïve T cells by repetitive stimulation with immature dendritic cells. The population described by Jonuleit *et al.* is not a naturally occurring population.

Particularly, Jonuleit *et al.* describes the removal of naïve $CD4^+$ cells from blood (p. 1214, 2nd col., 4th paragraph) and shows the results of a cell surface marker

assay (in Figure 4). Jonuleit *et al.* describes in detail how "alloreactive CD4+ T cell lines" were generated by "repetitive stimulations with iDCs or mDCs from the same donor" (page 1215, first paragraph). The title of Jonuleit *et al.* ("Induction of Interleukin 10-producing, Nonproliferating CD4+ T Cells with Regulatory Properties by Repetitive Stimulation with Allogeneic Immature Human Dendritic Cells") further emphasizes that this reference teaches the production of cells having the specified properties rather than identifying, monitoring and/or removing of a natural population from human blood. Thus, Jonuleit *et al.* teaches a method of generating a particular cell population *in vitro* and does not teach the identifying, monitoring and/or removing of a natural population of human $CD4^+$ $CD25^+$ regulatory T cells from human blood, as is presently claimed.

With regard to newly added claims 28-32, applicants particularly note that Jonuleit *et al.* does not teach or suggest that $CD4^+$ T cells removed from blood have regulatory properties but rather teaches that cells having regulatory properties can be produced *in vitro* via repetitive stimulations with dendritic cells.

In view of these differences between Jonuleit *et al.* and the claimed subject matter, applicants respectfully submit Jonuleit *et al.* does not anticipate the claimed subject matter. Applicants therefore respectfully request that the rejection of claims 12 and 24-27 on this basis be withdrawn, and further, not be applied to newly added claims 28-32.

B. Horwitz *et al.*

Claims 12 and 24-27 stand rejected by the Patent Office under 35 U.S.C. § 102(e) as being anticipated by Horwitz *et al.* Applicants respectfully disagree with the assertions of the Patent Office and traverse the rejection.

Applicants note that claim 12 (and thus also claims 24-27, which depend from claim 12) has been amended to recite that the human blood is contacted with ligands specifically binding to the CD4 and CD25 entities on the T cells. Moreover, Horwitz *et al.* does not teach the claimed subject matter of a method to identify, monitor and/or remove $CD4^+$ $CD25^+$ regulatory T cells from human blood. Instead, Horwitz *et*

al. at best teaches the induction of regulatory T cells from $CD4^+$ T cells by stimulation with TGF-β. The population described by Horwitz *et al.* is not a naturally occurring population.

Particularly, Horwitz *et al.* (col. 7, lines 49-65) teaches the "activation of naïve $CD4^+$ T cells in the presence of TGF-β..." and confirms that these activated cells express CD25 (see also Figure 10 and legend in col. 7, line 66 through col. 8, line 3). Only after treatment and induction with TGF-β are the (induced) cells separated into $CD25^+$ and $CD25^-$ fractions (see, *e.g.*, col. 7, line 66 through col. 8, line 3; see also col. 8, lines 11-18). Results from these experiments are shown in Figure 9 (see col. 21, lines 34-39; col. 22, lines 10-14) and Figure 10A, which also shows results from cells "primed with allogeneic stimulator cells" (see the figure legend for Figure 10A in col. 8, lines 1-5).

It is also not clear that Horwitz *et al.* actually demonstrates the use of human cells. Instead, Horwitz *et al.* appears to describe experiments with rodents. The word "human" is only used a few times in the specification, and most of the examples disclosed by Horwitz *et al.* describe the use of cells from "patients," a term which includes rodents (see, *e.g.*, col. 10, lines 66-67). The only experiment specifically described as using human cells involves $CD8^+$ cells (see, *e.g.*, col. 6, lines 61-63). Thus, it is not clear that Horwitz *et al.* teaches any human cell populations.

With regard to newly added claims 28-32, applicants particularly note that Horwitz *et al.* does not teach or suggest that $CD4^+$ T cells removed from blood have regulatory properties but rather teaches that cells having regulatory properties can be produced via stimulation with TGF-β.

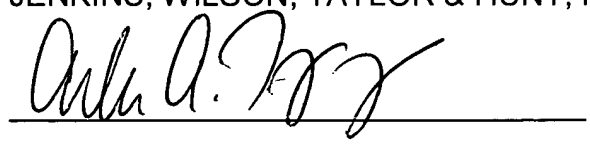
In view of these differences between Horwitz *et al.* and the claimed subject matter, applicants respectfully submit Horwitz *et al.* does not anticipate the claimed subject matter. Applicants therefore respectfully request that the rejection of claims 12 and 24-27 on this basis be withdrawn, and further, not be applied to newly added claims 28-32.

DEPOSIT ACCOUNT

A check in the amount of $60.00 representing a one-month Petition for Extension of Time fee for a small entity is enclosed herewith in connection with the filing of this correspondence, and the Commissioner is hereby authorized to charge any additional fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: September 1, 2006 By: 

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Response to 35 U.S.C. § 112, Second Paragraph Rejections

Claims 12 and 24-27 stand rejected by the Patent Office under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. Applicants respectfully disagree with the assertions of the Patent Office and traverse the rejection.

Applicants note that claim 12 (and thus also claims 24-27, which depend from claim 12) has been amended to recite that the human blood is contacted with ligands specifically binding to the CD4 and CD25 entities on the T cells. Further, claim 24 has been amended to correctly refer to "CTL-A4", rather than "TL-4A".

Support for newly added claims 28-32 is particularly described hereinbelow. In view of this support, applicants believe that these new claims are fully described by the present specification and meet the requirements of 35 U.S.C. § 112 as well.

In view of these amendments, Applicants respectfully request that the rejection of claims 12 and 24-27 on this basis be withdrawn, and further, not be applied to newly added claims 28-32.

New Claims

New claims 28-32 have been added. Support for the new claims can be found in the working examples and throughout the specification, including: on page 1, lines 5-9; on page 3, line 21 through page 4, line 15; page 7, lines 4-7; and page 22, line 21 through page 23, line 8. Particular support for the limitations of the new claims also includes the following: for claim 29, on page 3, line 32 through page 4, line 11; for new claim 30, e.g., in working Example 3 beginning on page 22 (see particularly page 23, lines 10-21); for new claim 31, in working Example 5 beginning on page 24, line 30; and for new claim 32, in working Example 4 on page 24 (see also results shown in Figure 4C).

As discussed hereinabove, it is respectfully submitted that new claims 28-32 are allowable over the prior art. No new matter is considered to have been added.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.